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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,391	10/28/2003	Jeffrey Isner	47624-CIP (71417)	6371

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/696,391	Applicant(s) ISNER ET AL.	
	Examiner Quang Nguyen, Ph.D.	Art Unit 1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 24 July 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *24 July 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *49-52,54-65 and 68*.

   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments are respectfully not found persuasive.

1. With respect to the 103 (a) rejection over Isner in view of Hammond and Dillmann, Applicant argues that the supporting Hammond reference describes methods for coating a synthetic vascular graft with endothelial cells, and such methods are clearly different from the claimed invention which recites methods for inducing blood vessels in myocardial tissue. Applicant argues that methods for increasing the number of endothelial cells that adhere to and coat a synthetic graft are distinctly different from the multifaceted biological processes that regulate blood vessel formation within a myocardial tissue. Additionally, Applicant argues that the endothelialization results obtained by Hammond fail to provide the requisite motivation to combine or the expectation of success to modify the methods of Isner by pointing out the undesirable side effects that could affect the long-term utility of the BMB grafts reported in example 1. Regarding to the supporting Dillmann reference, Applicant argues basically that Dillmann fails to remedy the deficiencies of the other references cited by the Examiner.

Please note that the rejection of record is a 103(a) rejection, and it appears that Applicant completely ignored the teachings of Isner. Isner teaches clearly that an angiogenic factor can be combined with other genes or their encoded gene products to enhance the activity of targeted cells in a method for enhancing blood vessel formation or an angiogenesis in an ischemic tissue, including ischemic cardiomyopathy or myocardial ischemia, in a mammal. Hammond teaches clearly that SCF, GM-CSF, G-CSF are capable of mobilizing bone-marrow derived endothelial cell progenitors or non-adherent CD34+ cells in the blood for enhancing the endothelialization of synthetic vascular grafts in a patient. Hammond also notes that CD34+ circulating cells in blood can participate in the repair of ischemic tissue (col. 3, lines 28-37). As already pointed out in the final rejection mailed on 3/22/2006, an ordinary skilled artisan would have been motivated to modify the method of Isner by further administering to the treated mammal with an effective amount of at least one of SCF, GM-CSF and G-CSF, or an effective fragment thereof because Hammond already demonstrated that the aforementioned cytokines are capable of mobilizing bone-marrow derived endothelial cell progenitors in the blood, and that this mobilization of endothelial cell progenitors would further enhance blood vessel formation or angiogenesis in an ischemic tissue in a mammal having a myocardial ischemia, and thus further optimizing the angiogenic therapeutic outcome.

With respect to the undesirable side effects in example 1 of the Hammond reference, please note that BMB grafts in example 1 were seeded with autologous bone marrow blood ex vivo prior to their implantation in vivo, these undesirable side effects were not observed in animals receiving G-CSF after the implantation of the graft (see at least examples 3 and 4). Thus, there is no teaching away whatever in the Hammond reference, particularly with respect to the main issue that SCF, GM-CSF and G-CSF are capable of mobilizing bone-marrow derived endothelial cell progenitors in the blood for enhancing endothelialization, and that Hammond also recognizes that CD34+ circulating cells in the blood can participate in the repair of ischemic tissue.

Regarding to the Dillmann reference, its teachings are used to supplement the teachings of both Isner and Hammond on the various means recited in the claims to monitor a cardiac function, and that these means are well-known and conventionally used by those of ordinary skill in the relevant art to monitor clinical signs of improvement in cardiac performance, particularly in the treatment of ischemic cardiomyopathy and/or myocardial ischemia.

2. With respect to the provisional obviousness-type double patenting rejection with the co-pending Application No. 10/714,574 in view of Dillmann, Applicant requests that this rejection is withdrawn pursuant to M.P.E.P 822.01, should this rejection will be the only rejection remaining in the instant application.

The provisional obviousness-type double patenting rejection is maintained because it is not the only remaining rejection in the instant application (please refer to the 103(a) rejection of record).

QUANG NGUYEN, PH.D
PATENT EXAMINER